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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,036	09/30/2002	Paul R. Sanberg	1372.623.PRCWOUS	5509

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
10/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/009,036	SANBERG ET AL.	
	Examiner	Art Unit	
	Daniel E. Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7,10,12-17,19,20 and 24-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7,10,12-17,19,20 and 24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Borlongan printout 1st page*.

DETAILED ACTION

1. The remarks and amendments filed 29 July 2010 have been entered. Claims 1-2, 4, 7, 10, 12-17, 19-20, 22, 24-31 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 July 2010 has been entered.

Withdrawn Rejections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. The objection to claim 23 is moot as the claim has been canceled.

B. The rejection under 35 USC 112, first paragraph for recitation of new matter is withdrawn in light of the amendments which change “about 6 million” to “at least 6 million”.

C. The rejections of record under 35 USC 103(a) are withdrawn in light of the new limitation “within three hours of cell preparation”, which appears in each of independent claims 1, 10, 13-15, 17, and 20. This newly-added limitation is addressed in the new rejections below.

New Rejections

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 2, 4, 17, 20, 22, 24-28, and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9) in view of Weiss (U.S. Patent 5,851,832), Grabowski (1994. Exp Neurol. 127(1):126-136), and Borlongan 1998 (NeuroReport 9:2837-2842, cited as reference 25 on IDS filed 15 November 2002). Note Borlongan qualifies as prior art as the reference was published on the internet on 12 August 1998, and is not by the present inventive entity. The first page of Borlongan, as downloaded from the journal's website, is attached here as it provides evidence of the date of publication.

Sanberg teaches that hNT cells, transplanted into the brains of rats who had experienced ischemia-inducing surgery a month earlier, are effective to ameliorate behavioral symptoms of stroke. Sanberg teaches that of the doses tested (5,000 – 40,000 cells administered to adult rats), 40,000 cells was the most effective and 5,000 and 10,000 cells were not effective; 20,000 cells per rat was partly effective. The reference therefore is on point to treating stroke with hNT cells; however Sanberg does not explicitly teach administering the cells to humans and does not teach administration of at least 6 million cells, or a plurality of sites as recited, or administering the hNT cells within three hours of preparing them as recited in claims 1, 17, and 20. Further Sanberg does not explicitly teach the specific locations within the brain as recited in claims 1 and 20 or the spacing (about 5 to 6 mm) recited in claim 2 and 31, or waiting at least three months between stroke and cell delivery as in claim 4.

Weiss teaches that when using neuronal cells derived from neural stem cells to treat stroke, 1 – 3 ul of cells at up 50 x 10^6 cells per ml were administered (see column 62 lines 15 – 40) to rats. This corresponds to up to 150,000 cells per animal. Assuming a weight of about 0.3 kg, this is a dose of 500,000 cells per kg of body weight. However Weiss does not teach hNT neuronal cells, does not explicitly teach "a plurality of brain area sites", as recited in claims 1 and 17 and does not explicitly teach treatment of humans who have experienced stroke at least 3 hours prior to treatment, as recited in claim 1.

Grabowski et al. teach another model of transplantation in which fetal cortex is grafted into the infarcted cortex of rats that having undergone middle cerebral artery occlusion (MCAO)

5-7 days, 3 weeks, or 8 weeks prior. The reference therefore is on point to treatment of stroke by administration of cells into the brains of affected patients. Grabowski teaches that when transplantation surgery is delayed, graft survival is significantly improved. These investigators conclude that a delay between lesion and transplantation is desirable in this stroke model. Additionally, Grabowski teaches treating rats that have undergone MCAO by administering cells in multiple brain areas. At p. 127, end of paragraph bridging the two columns, Grabowski teaches giving the cells to at least two different sites, which are 3 mm apart in the dorso-ventral plane. This is relevant to claims 1-2 and 31, and suggests that when cells are delivered to subjects suffering from stroke multiple sites of administration are routinely used. While Grabowski suggests that delay between the time of stroke and transplantation surgery actually improves out come, the reference does not explicitly teach waiting at least 3 months as recited in claim 4, and does not teach hNT neuronal cells.

Borlongan teaches treating rats with middle cerebral artery occlusion by administering hNT cells. Like the reference by Sanberg cited above, the reference by Borlongan teaches that animals that received 40,000 cells improved, and the reference also refers to this as a rodent model of stroke (p. 2837 second paragraph). Borlongan explicitly teaches that for hNT cells, "the cell viability dramatically decreases within a few hours following thawing" (p. 2838, second column, first complete paragraph; see also p. 2842 first complete paragraph). This is on point to claims 1 and 17, specifically the newly-added limitation “within three hours of cell preparation”, as Borlongan provides guidance to use the cells “within a few hours”. However Borlongan does not explicitly teach administering the cells to humans and does not teach administration of at least 6 million cells, or a plurality of sites as recited in claims 1 and 17. Further Sanberg does not explicitly teach the specific locations within the brain as recited in claim 1 or the spacing (about 5 to 6 mm) recited in claim 2, or waiting at least three months between stroke and cell delivery as in claim 4.

It would have been obvious to one of ordinary skill in the art to modify the methods of Weiss, who teaches treatment of stroke by administering neural stem cells and indicates that such treatments will also be effective in humans, by substituting the hNT cells of Sanberg and Borlongan and by using the cells as rapidly as possible following preparation, as taught by Borlongan. Additionally, it would have been obvious to one of ordinary skill in the art to use about 6 million cells, given the teachings of Sanberg and Borlongan. The motivation to do modify the methods of Weiss would be to effectively treat stroke in humans. It would have been

reasonable to expect success as well. Selection of the specific areas within, inferior, and superior to the stroke area as in claims 1 and 20, would have been obvious to one of ordinary skill in the art as an artisan of ordinary skill in this field is a neurosurgeon who would optimize placement of therapeutics for any given stroke patient; see also Weiss column 22 line 56 - column 23 line 20, column 24 lines 7-31, column 64 lines 14-21. Note also Grabowski teaches administration within the infarct area. Thus the specific limitations in claims 1 and 22 as to the areas within, superior, and inferior to the stroke would have been obvious one of ordinary skill in the art.

Claim 20 is included in this rejection as well. Note that the claim recites no limitations beyond those previously addressed in this rejection. The references render obvious administering to more than one brain site (which is indistinct from a plurality of brain sites as recited in claim 1), to a human who has had a stroke, at least 6 million hNT cells. hNT cells are neural cells and are encompassed by claims 27-28. While the references do not explicitly teach that morbidity would be decreased over at least a year, that is not an active step recited by claim 20 but rather is an effect which will occur once the method is performed. Claim 24 is included as sterotactic injection would have been obvious; see Weiss column 24 lines 13-20. Claims 25-26 are included as the claim recites outcomes which will happen upon performing the method which is obvious, and does not recite any additional starting materials or method steps. As described above, the references provide both a motivation to perform the methods with a 3-month delay and a reasonable expectation of success, as in claim 30.

In the remarks filed 29 July 2010 applicant argued that the office has failed to provide evidence supporting the official notice taken with respect to weights of rats and humans. Although applicant did not point to any particular errors the examiner had made in determining what constitutes an average weight for a rat or human, applicant appears to be requesting data backing up the examiner's assumption as to the weights (remarks, p. 9). On p. 4 final paragraph of the office action mailed 6 February 2009, the examiner asserted that rats weigh approximately 300g (0.3 kg), and that humans weigh approximately 75 kg. These facts are supported by the following references:

1) Charles River Laboratories, price and growth chart for Sprague-Dawley rats. Note that prices are given for males up to 350 grams, and for females up to 250 grams. Furthermore the growth chart on the right shows that while growth continues through all time points listed, there is a plateau in weight gain at about 11 weeks, when males weigh over 300 g and females

weigh over 200 g. The data indicate that the examiner's assertion that a rate weighs about 300 g is correct.

2) Center for Disease Control and Prevention, Advance Data From Vital and Health Statistics, Number 347 October 2004. The reference provides historical review of human body weights in the United States. Note in particular Table 6 on page 8 for weights of adults. Weights are given for each decade from 20-60, and for patients 60-74 years old. While any single age group studied at any one of the periods listed (from 1960 through 2002) could be used as a reasonable estimate of body weight, the examiner notes that 75 kg (which converts to 165 lbs.) is about the average weight of males from 1960-62 and near the maximum weight of females from 1999-2002.

These data support the office's assertions as to weight of humans. While the Office did set forth an exact average weight, the numbers used by the examiner in his calculations (0.3 kg for a rat and 75 kg, or 165 lbs. for a human) are not atypical.

Applicant also argues that the present inventors used 6 million cells, whereas scaling up in the manner suggested by the examiner would lead to administration of "at least 10 million cells" (remarks, p. 10). The examiner agrees entirely and notes that applicant is not claiming administration of 6 million cells; applicant is claiming administration of 6 million cells or more ("at least 6 million"). Thus while the references point one of ordinary skill in the art to administer more than 6 million cells, this is exactly what applicant is claiming.

5. Claims 1 – 2, 4, 17, 20, 22, 24-28, and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9) in view of Weiss (U.S. Patent 5,851,832), and Grabowski (1994. Exp Neurol. 127(1):126-136)

The examiner acknowledges that the reference by Borlongan was published less than a year prior to the filing of the provisional application in the present case, and that should applicant successfully argue that the reference by Borlongan either is not "by another" or provide evidence that applicant was in possession of the invention prior to the publication of Borlongan, the rejection may be withdrawn. Therefore in the interest of compact prosecution a second rejection is being made, without relying on Borlongan, to indicate that the claimed invention would have been obvious to one of ordinary skill in the art even without the guidance from Borlongan.

The teachings of Sanberg, Weiss, and Grabowski are all set forth above. While the references render obvious a method of administering at least 6 million hNT cells to humans suffering from stroke, none of the references specifically teaches administering the cells within three hours of preparation as claimed. Nevertheless it would have been obvious to one of ordinary skill in the art to do so, as it is generally obvious to optimize protocols; see for example MPEP § 2144.05(II). Selecting a specific time point, such as less than three hours, would easily be arrived at by routine experimentation. Furthermore one of ordinary skill in the art would immediately recognize that it would be preferable to administer any preparation comprising cells sooner rather than later, as the cells would be more likely to be alive closer to the time of their preparation.

6. Claims 1-2, 4, 17, 20, 22, and 24-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg in view of Weiss and Grabowski as applied to claims 1-2, 4, 17, 20, 22, 24-28, and 30-31 above, and further in view of Larazov-Spiegler 1996 (FASEB J. 10:1296-1302).

The reasons why claims 1 – 2, 4, 17, 20, 22, 24-28, and 30-31 would have been obvious to one of ordinary skill in the art are set forth above. However none of the cited references explicitly teaches coadministering macrophages that have been activated by exposure to peripheral nerve cells as recited in claim 29.

Larazov-Spiegler teaches that administering macrophages that have been exposed to a peripheral nerve, in particular sciatic nerve segments, is therapeutic for damaged CNS neurons. See for example abstract, as well as paragraph spanning pp. 1297 - 1298. This is on point to claim 29. However Larazov-Spiegler does not teach treating stroke in humans, as required by independent claim 20.

It would have been obvious to one of ordinary skill in the art to modify the methods rendered obvious by Weiss in view of Sanberg 1997 and Graboswki to include administration of macrophages activated by peripheral nerves, as taught by Larazov-Spiegler, thereby arriving at the invention of claim 29. Doing so would have been obvious to one of ordinary skill in the art, as each product (the porcine fetal neurons and the activated macrophages) was known to be effective for treating damaged CNS tissue, so coadministering them would have been obvious.

Applicant argued that if the independent claims are not obvious, then the dependent claims cannot possibly be obvious. The examiner agrees with this reasoning, but notes that the

independent claim is still rejected as obvious. Applicant did not separately traverse the examiner's determination that the specific limitations of claim 29 would have been obvious to one of ordinary skill in the art given the teachings of Larazov-Spiegler.

7. Claims 7, 10, 12-17, and 19-20, 22, 24-28, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg (1996. Soc. Neurosci. Abstr. 22(1-3):578, abstract 232.9) in view of Sanberg (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9), Weiss (U.S. Patent 5,851,832), Uchida (1995. Exp. Neurol 132:194-208), and Borlongan 1998 (NeuroReport 9:2837-2842, cited as reference 25 on IDS filed 15 November 2002).

Sanberg 1996 teaches that transplantation of human teratocarcinoma neuronal cells (hNT) to ischemic rats produces recovery of motor function and passive avoidance behavior. The reference is therefore on point to claims 10, drawn to strokes which interfere with movement. Adult rats were subjected to ischemic embolism by middle cerebral artery occlusion were allowed to recover for one month before being tested for asymmetric motor behavior (elevated body swing task, EBST, which is a movement test) and passive avoidance behavior, a cognitive test. Sanberg 1996 teaches that one month following transplantation of hNT cells, significant recovery in both the EBST and passive avoidance tasks was observed in groups that received hNT cells as compared to controls. Control animals were reported to show no behavioral recovery. Sanberg concludes that transplantation of hNT cells into the infarcted striatum of rats having stroke improves motor and cognitive deficits associated with such ischemia, and therefore is on point to claims 10, 12, 13, and 15. As the EBST requires sensory input, the reference is on point to claim 14 as well. Additionally, as speech is known to be one of several motor components affected by stroke, the reference is also on point to claim 7. However Sanberg does not teach administration to humans and does not explicitly teach administration of at least 6 million cells as recited in claims 7, 10, 13-15, and 17 and does not explicitly teach sterile compositions. Furthermore the reference does not teach using the cells within three hours of preparation as recited in claims 7, 10, 13-15, and 17, and does not teach administering the cells to the specific locations within, superior to, and inferior to the infarct recited in claims 7, 10, and 13.

Sanberg 1997 teaches that hNT cells, transplanted into the brains of rats who had experienced ischemia-inducing surgery a month earlier, are effective to ameliorate behavioral symptoms of stroke. Sanberg 1997 teaches that of the doses tested (5,000 – 40,000 cells

administered to adult rats), 40,000 cells was the most effective and 5,000 and 10,000 cells were not effective; 20,000 cells per rat was effective in some but not all subjects. The reference therefore is on point to treating stroke with hNT cells; however Sanberg 1997 does not explicitly teach administering the cells to humans and does not teach administration of at least 6 million cells and does not explicitly teach sterile compositions. The Sanberg 1997, like the Sanberg 1996 reference, does not teach using the cells within three hours of preparation as recited in claims 7, 10, 13-15, and 17, and does not teach administering the cells to the specific locations within, superior to, and inferior to the infarct recited in claims 7, 10, and 13.

Weiss ('832 patent) teaches a method for the treatment of neurodegenerative diseases comprising administering to a mammal (such as a human) neural stem cell progeny (which may also be derived from humans) that have been induced to differentiate into neurons and/or glia (column 11, lines 13-17). The patent teaches that acute brain injuries (such as stroke) often result in the loss of neural cells, leading to inappropriate functioning of the affected brain region (column 3, lines 22-24). As disclosed by the '832 patent, treatment of neurodegenerative disease using progeny of human neural stem cells involves first having the patient undergo a CT scan to determine the coordinates of the region to receive the transplant, then using injection cannula to inject the tissue suspension to the correct coordinates (column 42, example 14). It would be an expected property of the injected cell compostion to be sterile if it was used therapeutically in humans. Note Weiss explicitly teaches collection of tissue by sterile technique (Example 14 among others) and administration of sterile saline (Example 15) as a control; thus it is reasonable that the cells administered in the same experiments are in fact in a sterile composition. Weiss teaches administration of progeny of neural stem cells to mice and rats by administering 1 – 3 ul of cells (column 62) at up to 50 x 10^6 cells per ml. This corresponds to up to 150,000 cells per animal. However Weiss does not teach administration of hNT cells as recited in claims 7, 10, 12 – 15, 17, and 19, and does not teach administration into the cisternae as recited in claim 16.

Borlongan teaches treating rats with middle cerebral artery occlusion by administering hNT cells. Like the reference by Sanberg references cited above, the reference by Borlongan teaches that animals that received 40,000 cells improved, and the reference also refers to this as a rodent model of stroke (p. 2837 second paragraph). Borlongan explicitly teaches that for hNT cells, "the cell viability dramatically decreases within a few hours following thawing" (p. 2838, second column, first complete paragraph; see also p. 2842 first complete paragraph).

This is on point to claims 7, 10, 13-15, and 17, specifically the newly-added limitation "within three hours of cell preparation", as Borlongan provides guidance to use the cells "within a few hours". However Borlongan does not explicitly teach administering the cells to humans and does not teach administration of at least 6 million cells, or a plurality of sites as recited in claims 7, 10, 13-15, and 17. Further Sanberg does not explicitly teach the specific locations within the brain as recited in claims 7, 10, and 13.

It would have been obvious to one of ordinary skill in the art to modify the method of Sanberg 1996, who teaches administration of hNT cells to animals with cognitive, sensory, and motor damage from strokes, by following the guidance set forth in Sanberg 1997, Weiss '832 patent, Uchida, and Borlongan. Sanberg 1997 provides guidance as to the effective dose; as set forth previously 20,000 - 40,000 cells given to a rat corresponds to more than 6 million cells administered to a human when scaled up to the larger weight of humans. Weiss provides guidance as to treatment of human patients suffering from stroke with neural cells. Additionally, Uchida provides the artisan with guidance to select intraventricular administration, which is on point to "into the cisternae" as recited in claim 16. The artisan would have been further motivated to inject the cells cisternally, not only because Uchida teaches that implanted neuronal cells can migrate some distance from their implantation site, but also because the an intracisternal injection can be performed without drilling into the skull and is therefore less invasive and would reasonably be expected to result in fewer potential complications. Uchida also provides the motivation to select additional cell types, including fetal non-human cells and neural stem cells which are present in the embryonic neural plate used (see p. 197 second column from Uchida); it is obvious to co-administer two treatments known to be effective for the same purpose. Here, both the hNT cells from Sanberg and the neural stem cells in the composition from Uchida are both known to be suitable for transplantation into brain for therapeutic purposes. Additionally it would have been obvious to one of ordinary skill in the art to treat stroke which "interferes with speech", as this is a type of motor disorder caused by stroke. Given that Sanberg teaches therapeutically treating rats with motor disorders caused by stroke following administration of hNT cells, it would have been obvious to one of ordinary skill in the art to treat human motor deficits, including those related to speech. Finally Borlongan provides guidance as to using the cells within three hours of preparation, as in claims 7, 10, and 13. Claim 19 is included in this rejection as Weiss teaches administering neural stem cells for treatment of stroke, so including these cells (i.e. concomitantly administering them) would have

been obvious as well. Claim 20 is included in this rejection as it is drawn to treating morbidity resulting in at least one of cognitive function, motor function, sensory, or speech function, and the reference by Sanberg 1996 teaches that administration of the cells improves several of these, including both cogntivie (passive avoidance) and motor (EBST) tasks. Claim 22 is included as selection of the specific regions within, inferior, and superior to the stroke would have been obvious to a skilled neurosurgeon.

Applicant argues that the examiner has not given sufficient weight to the "improving speech" limitation recited in claim 7, as speech involves both motor and cognitive components. The examiner respectfully disagrees. First, "speech" is not the same as language; impaired speech need not necessarily be indicative of impaired language ability or impaired cognition. A patient's cognition and language production capabilities may be just fine, yet the patient may nonetheless have impaired speech due to a stroke which affects the motor regions controlling the lips, mouth, tongue, and throat. Second, even if one were to construe a deficit in "speech" as necessarily having deficits in both language and cognitive abilities, the method of claim 7 would still be obvious over the cited references, as Sanberg 1996 shows recovery in tasks which require both motor (EBST) and behavioral (passive avoidance) components. Thus it would be reasonable to expect that the same treatment would have the same effects, namely improving both motor and cognitive aspects of tasks when given to humans. Claim 24 is included as sterotactic injection would have been obvious; see Weiss column 24 lines 13-20. Claims 25-26 are included as the claim recites outcomes which will happen upon performing the method which is obvious, and does not recite any additional starting materials or method steps. As described above, the references provide both a motivation to perform the methods with a 3-month delay and a reasonable expectation of success, as in claim 30.

8. Claims 7, 10, 12-17, and 19-20, 22, 24-28, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanberg (1996. Soc. Neurosci. Abstr. 22(1-3):578, abstract 232.9) in view of Sanberg (1997. Soc. Neurosci Abstr 23(1-2):346, abstract 140.9), Weiss (U.S. Patent 5,851,832), and Uchida (1995. Exp. Neurol 132:194-208).

The examiner acknowledges that the reference by Borlongan was published less than a year prior to the filing of the provisional application in the present case, and that should applicant successfully argue that the reference by Borlongan either is not "by another" or provide evidence that applicant was in possession of the invention prior to the publication of

Borlongan, the rejection may be withdrawn. Therefore in the interest of compact prosecution a second rejection is being made, without relying on Borlongan, to indicate that the claimed invention would have been obvious to one of ordinary skill in the art even without the guidance from Borlongan.

The teachings of Sanberg 1996, Sanberg 1997, Weiss, and Uchida are all set forth above. While the references render obvious a method of administering at least 6 million hNT cells to humans suffering from stroke, none of the references specifically teaches administering the cells within three hours of preparation as claimed. Nevertheless it would have been obvious to one of ordinary skill in the art to do so, as it is generally obvious to optimize protocols; see for example MPEP § 2144.05(II). Selecting a specific time point, such as less than three hours, would easily be arrived at by routine experimentation. Furthermore one of ordinary skill in the art would immediately recognize that it would be preferable to administer any preparation comprising cells sooner rather than later, as the cells would be more likely to be alive closer to the time of their preparation.

Conclusion

9. No claim is allowed.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Trojanowski 1993 (Experimental Neurology 122, 283-294, cited on IDS filed 15 November 2002). The reference teaches administration of NT2 cells into the brains of rats. These cells are from a cell line which is the parent of cell line hNT (specification p. 5 lines 9-10). Trojanowski indicates that frozen cells can be administered, and teaches that this is to be done immediately after thawing (p. 284 last complete paragraph). Cells that had been frozen remained viable following transplantation (p. 289 first complete paragraph). This suggests to one of ordinary skill in the art that cells to be implanted in brain should be used soon after thawing or other preparation, and therefore gives guidance toward administering the cells within three hours of preparation as recited in the independent claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel E. Kolker whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E Kolker/
Primary Examiner, Art Unit 1649
October 5, 2010